UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,772	07/12/2001	Masahiro Iwamoto	46124-5001-01	1361

9629   7590   01/15/2003

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EXAMINER
SCHNIZER, HOLLY G

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 09/902,772	Applicant(s) IWAMOTO ET AL.
	Examiner Holly Schnizer	Art Unit 1653

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _01 November 2002_ .

2a)☐ This action is **FINAL.**   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1,5 and 20-39_ is/are pending in the application.

　　4a) Of the above claim(s) _1,5,20-31,33,35 and 39_ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _32,34 and 36-38_ is/are rejected.

7)☒ Claim(s) _34_ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

　　Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

　　If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

　　a)☐ All b)☐ Some * c)☐ None of:

　　　1.☐ Certified copies of the priority documents have been received.

　　　2.☐ Certified copies of the priority documents have been received in Application No. _____ .

　　　3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

　　* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

　　a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _6_ .

4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

Applicant's election of Group II, Claims 32, 34, and 36-38, drawn to

polynucleotides encoding C-11 in Paper No. 10 is acknowledged. Because applicant

did not distinctly and specifically point out the supposed errors in the restriction

requirement, the election has been treated as an election without traverse (MPEP

§ 818.03(a)).

Therefore, Claims 1, 5, and 20-39 are pending, Claims 1, 5, 20-31, 33, 35, and

39 are withdrawn from consideration as being drawn to non-elected subject matter, and

Claims 32, 34, and 36-38 have been considered in this Office Action.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created
doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the
unjustified or improper timewise extension of the "right to exclude" granted by a patent
and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11
F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225
USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA
1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*,
418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be
used to overcome an actual or provisional rejection based on a nonstatutory double
patenting ground provided the conflicting application or patent is shown to be commonly
owned with this application. See 37 CFR 1.130(b).
Effective January 1, 1994, a registered attorney or agent of record may sign a
terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with
37 CFR 3.73(b).

Claims 32 and 34 are rejected under the judicially created doctrine of

obviousness-type double patenting as being unpatentable over claims 1-2 of U.S.

Patent No. 6,294,354.

An obviousness-type double patenting rejection is appropriate where the

conflicting claims are not identical, but an examined application claim is not patentably

distinct from the reference claim(s) because the examined claim is either anticipated by,

or would have been obvious over, the reference claim(s). See e.g., In re Berg, 140 F.3d

1428, 46USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d

2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, claims 1 and 2 of U.S. Patent No. 6,294,354 recites a nucleic acid

encoding a C11 protein comprising the amino acids as set forth in SEQ ID NO:2 and the

nucleic acid sequence of SEQ ID NO:1. These nucleic acids differ from that of the

composition comprising an c-erg gene claimed in Claims 32 and a composition

comprising a C-11 gene or a c-erg gene of Claim 34 of the present application only in

that SEQ ID NO:1 is missing nucleotides 655-735 of the c-erg gene. However, Patent

No. 6,294,354 also teaches the sequence of the c-erg gene and teaches that both C-11

and c-erg, when introduced into osteoblasts, inhibit calcification (see abstract of the

patent). Therefore, it would have been obvious to modify the C-11 sequence to add the

additional nucleotides 655-735 of the c-erg gene in order to express the c-erg protein for

use in studying cartilage morphogenesis. One of ordinary skill would have been

motivated to express both C-11 and c-erg in order to better understand how the protein

structures affect cartilage morphogenesis and to explore the differences in tissue

expression of the two genes in order to better understand the role of the erg genes

during chicken embryogenesis.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that

form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by

Dhordain et al. (Mech. Dev. (1995) 50: 17-28; cited in IDS of Paper No. 6).

Dhordain et al. teach the cloning of the chicken erg gene (ck-erg) (see lines 6-7

of abstract). The erg gene composition of Dhordain et al. appears to be

indistinguishable from the pharmaceutical compositions of present Claims 32 and 34.

The erg gene disclosed in Dhordain et al. appears to have a sequence identical to SEQ

ID NO: 1 and 3 of the present invention except that it contains an extra 81 nucleotides

from position 655-735 of SEQ ID NO:1 (see sequence alignment attached to this Office

Action).

Claim Rejections - 35 USC § 112

***It is noted that the following enablement rejection contains two separate issues.

Claims 32 and 34 are deemed to lack enablement because of the intended use of the

claimed compositions in methods of gene therapy. Claim 36 lacks enablement because the primer of (b) comprising the complement of nucleotides 645-662 as set forth in SEQ ID NO:1 (as required in the last lines of the claim) could not be used to amplify the nucleic acid encoding the protein having the sequence of SEQ ID NO:4. The rejections have been separated into two parts and are as follows:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: the nature of the invention; the breadth of the claims; the predictability or unpredictability of the art ; the amount of direction or guidance presented; the presence or absence of working examples; the quantity of experimentation necessary; the state of the prior art; and, the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Breadth of the Claims

The claims are drawn to <u>pharmaceutical</u> compositions comprising genes. Thus, the claims encompass the <u>intended use of the claimed compositions in gene therapy</u>.

Nature of the Invention

A review of the Specification appears to indicate that the invention is the discovery of a "novel isoform of the c-erg gene (herein referred to as 'C-11 gene' or 'C11 gene') which is an erg gene derived from chicken" (p. 5, lines 1-5 of Specification).

The Amount of Direction or Guidance Presented and the Presence or Absence of Working examples:

The present Specification does not provide any working examples of methods of gene therapy using the disclosed nucleotide sequences and does not provide any guidance as to any protocols for using the disclosed sequences in any gene therapy methods.

State of the prior art and relative skill of those in the art

At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by recently published reviews. Verma et al (Nature 389: 239-242, 1997) teach that "there is still no single outcome that we can point to as a success story (p. 239, col 1). The authors state further, "Thus far, the problem has been the inability to deliver genes efficiently and to obtain sustained expression" (p.239, col. 3). Anderson (Nature 392:25-30, 1998) confirms the unpredictable state of the art, stating that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease" (p. 25, col. 1) and concluding, "Several major deficiencies still exist

including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered" (p.30). More recently, Romano et al (Stem Cells 18:19-39, 2000) reviewed the general state of gene therapy, and found that the problems relating to gene delivery and expression discussed above persisted. See entire document, especially, last sentence of abstract; last sentence of column 1 on page 20 to column 2, line 6; page 21, column 1, lines 1-9 and 18-21; sentence bridging columns 1 and 2 on page 21; and first sentence of last paragraph on page 21. This idea was echoed by Somia and Verma (Nature Reviews/Genetics 1: 9199, 11/2000), who noted that delivery vehicles still represented the Achilles heel of gene therapy, and that no single vector existed that had all of the attributes of an ideal gene therapy vector. See page 91, column 1, lines 5-13 of first paragraph.

The predictability or unpredictability of the art

The art of gene therapy is highly unpredictable as evidenced by the problems discussed in the paragraph above.

In consideration of each of the above factors, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

The examiner notes that this enablement rejection can be overcome by deleting the term "pharmaceutical".

Claims 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing

subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to

make and/or use the invention.

Claim 36 encompasses a nucleic acid which is complementary to at least a

portion of a nucleic acid encoding a C-11 protein wherein the nucleic acid can be

selected from (b) a nucleotide primer capable of amplifying a nucleic acid encoding a

protein comprising amino acids derived from SEQ ID NO:4 wherein the complementary

nucleic acid (b) comprises the complement of nucleotides 645-662 as set forth in SEQ

ID NO:1. As stated in the Specification (p. 9), the C-11 gene (SEQ ID NO:1) lacks

nucleotides 655-735 of c-erg (SEQ ID NO:3 which encodes SEQ ID NO:4). Therefore,

it is impossible to use a primer for nucleotides 645-662 as set forth in SEQ ID NO:1 to

amplify the polynucleotide encoding the protein of SEQ ID NO:4 since the primer

sequence lacks nucleotides that are part of the sequence that encodes SEQ ID NO:4

(see sequence alignment attached to this Office Action for an example of a comparison

of the C-11 sequence (SEQ ID NO:1) to the c-erg sequence (Db sequence;

representative of SEQ ID NO:3 which encodes SEQ ID NO:4).

Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention.

It appears that the specific nucleic acids claimed (those selected from the group

of parts (a), (b), or (c) that comprise the complement of nucleotides 645-662 of SEQ ID

NO:1 constitute new matter. Claim 36 was added in the Second Preliminary

Amendment filed September 6, 2001. The Specification as originally presented does not

appear to describe primers or probes comprising specifically the complement of

nucleotides 645-662 of SEQ ID NO:1. Correction is required.

Conclusions
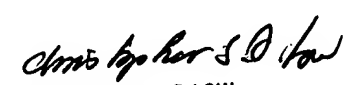
No Claims are allowable.

Any inquiry concerning this communication or earlier communications from the
examiner should be directed to Holly Schnizer whose telephone number is (703) 305-
3722. The examiner can normally be reached on Monday through Wednesday from 8
am to 5:30 pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's
supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone
numbers for the organization where this application or proceeding is assigned are (703)
308-4242 for regular communications and (703) 308-4242 for After Final
communications.
Any inquiry of a general nature or relating to the status of this application or
proceeding should be directed to the receptionist whose telephone number is (703 308-
0196.

Holly Schnizer
January 13, 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

RESULT 4

GGERG		
LOCUS	GGERG	1516 bp mRNA linear VRT 27-APR-1995
DEFINITION	G.gallus ERG mRNA.	
ACCESSION	X77159	
VERSION	X77159.1 GI:790439	
KEYWORDS	ERG gene.	
SOURCE	chicken.	
ORGANISM	Gallus gallus	

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Archosauria; Aves; Neognathae; Galliformes; Phasianidae;
Phasianinae; Gallus.

REFERENCE   1 (bases 1 to 1516)
AUTHORS   Dhordain,P., Dewitte,F., Desbiens,X., Stehelin,D. and
            Duterque-Coquillaud,M.
TITLE   Mesodermal expression of the chicken erg gene associated with
            precartilaginous condensation and cartilage differentiation
JOURNAL   Mech. Dev. 50 (1), 17-28 (1995)
MEDLINE   95329425
PUBMED   7605748
REFERENCE   2 (bases 1 to 1516)
AUTHORS   Duterque-Coquillaud,M.
TITLE   Direct Submission
JOURNAL   Submitted (17-JAN-1994) M. Duterque-Coquillaud, CNRS UA 1160,
            Oncologie Moleculaire, Institut Pasteur, 1 rue Calmette, 59019
            Lille, FRANCE

FEATURES   Location/Qualifiers
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                     QNIDGKELCKMTKDDFQRLTPSYNADLILLSHLHYLRETPLPHLTSDDVDKALQNSPRL
                     MHARNTGGATFIFPNTSVYPEATQRITTRPDLPYEQARRSAWTHSHSPTQSKRATOPSS
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BASE COUNT   458 a   392 c   327 g   339 t
ORIGIN

Query Match   92.9%; Score 1344; DB 5; Length 1516;
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Matches 1435; Conservative 0; Mismatches 0; Indels 81; Gaps 1;

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Qy      1 GAATTCCCGGACGACGAATAATTAATTATTAGCAATTAATTAGCGATCAATAATCTTGATCACA    60
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Qy     61 TTATGGCAAGCACTATTAAGGAAGCAATTATCAGTGGTGGTGAGTGAGGACCAGTCCTTGTTTG   120
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Qy    121 AGTGTGCCTACGGATCCGCCCCCCACCTTGCAAAGACAGAAATGACAGCCCTCTTCTTCCAGTG   180
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Qy    481 GGCAGTGGCTGGAGTGGAGTGGGGAAGAAGAGATATGGGTCTTCCAGACGTGGACATCTTGTTGT   540
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Qy    601 CGCCGAGCTATAACGGCAGATATCCTCCGTGCACACCTACACTCACTACT----   654
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Qy    655 --------------------------GTCCTCT-   654
                                    |||||||
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Qy    661 TTCCACATTTGACTTCAGATGATGTTGAATAGGCCTTACAAAACTCTCCACGGTTAATGC   720
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Qy    760 GGACGAGTCACAGCCATCCCCACTCACTCAAAAGCTACCCAACCATCATCTTCAACAGTGC   819
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Qy    820 CCAAAAACAGAAGACACCAGCCGTCCTCAGTTAGATCCTTATCAGATTCTTGGACGGACCAGCA   879
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Qy    880 GCCGTCTTGCAAAATCCAGGGAGAGTGGGCAGAGATACAGTCTATGGCAGCTTCCTACTTC   939
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Qy    940 TGTCGGACAGCTCCAACTCCAAACTGCATCACCTGGGAGGCCACAAATGGGGAGGGTTCAAGA   999
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Qy   1000 TGACAGACCCTGATGAAGTGGCTCGGCGGTTGGGAGGGAGGGAGGGAGAAGAGAAGAGATGA   1059
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Qy   1060 ACTATGACAAAACTCAGCCGTTGCACTTCGCTACTACTATGACAAAATATATTATGACTAAAG   1119
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Qy   1120 TTCATGTGGTAAACGCTATGCCTACACAAATTGATTTCCACGGAAATCGCTCAGCCCTCAGC   1179
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Qy   1180 CTCACCCTCAGAATCATCATTGTACAAAATACCCATCAGAGACCTCCCTACATGAGTTCCT   1239
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Qy   1240 ACCATGCACACCCCAGAGAAGATGAACTTTGTAGCTCCCCATCCCCTGCTTGCCGGTAA   1299
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Db   1261 CTCACCCTCAGAATCATCATTGTACAAAATACCCATCAGAGACCTCCCTACATGAGTTCCT   1320
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RESULT 5

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LOCUS       AB031088                1808 bp    mRNA    linear   ROD 07-AUG-2001
DEFINITION  Rattus norvegicus VESP14 mRNA for vascular endothelial cell
            specific protein 14, complete cds.
ACCESSION   AB031088
VERSION     AB031088.1  GI:15128488
KEYWORDS    .
SOURCE      Rattus norvegicus
ORGANISM    Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae;
            Rattus.
REFERENCE   1  (bases 1 to 1808)
  AUTHORS   Aoki,T., Toyoda,H., Nishimoto,S., Tawara,J., Ukai,Y. and
            Komurasaki,T.
  TITLE     Identification of VESP14,a vascular endothelial cell specific
            protein
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 1808)
  AUTHORS   Aoki,T., Toyoda,H., Nishimoto,S., Tawara,J., Ukai,Y. and
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  TITLE     Direct Submission
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            Fax:048-652-7254)
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